Efficacy and Safety of Tocilizumab in Patients with COVID-19: A Systematic Review and Meta-Analysis.

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Abstract

Background Tocilizumab (TCZ) is an anti-interleukin-6 antibody that has been used to treat patients with 2019 coronavirus disease (COVID-19). Numerous retrospective studies have shown beneficial treatment efficacy. Several recent randomized clinical trials have questioned the efficacy of TCZ in patients with COVID-19. Therefore, we performed an updated systematic review and meta-analysis to explore the effectiveness and safety of tocilizumab recently used for treating patients with COVID-19.

Methods Randomized clinical trials (RCTs) and comparative studies that compared the outcomes between TCZ and standard of care (SOC) were analysed. PubMed, EMBASE, and the Cochrane Library (inception to November 20, 2020) were systematically searched. Primary outcomes included mortality and the rate of requirement for mechanical ventilation (MV). In addition, several subgroup analyses stratified by disease severity, publication type and TCZ administration were performed.

Results Three RCTs, twenty-one cohort studies and nine case-control studies including 11,206 patients were finally included. The TCZ group included 2,794 patients (24.93%) and the SOC group included 8,412 patients (75.07%). The mortality rate (>14 days) of the TCZ group, 29.63% (590/1,991), was lower than the SOC group, 41.51% (2,380/5,734) (OR 0.64, 0.57 to 0.73; $p < 0.00001$). However, no significant difference in 14-day mortality rates was observed between the two groups (13.53% vs 22.92%, $p = 0.21$). Meanwhile, the rate of MV was significantly decreased in the TCZ group compared with the SOC group (OR 0.42, 0.22 to 0.83; $p = 0.01$). According to the results of the subgroup analysis stratified by disease severity, TCZ only reduced the mortality rate for critical patients with COVID-19 compared with SOC (OR 0.60, 0.52 to 0.71; $P < 0.00001$), particularly for patients in the intensive care unit (ICU) or patients requiring MV. No statistically significant increase was recognized in the rates of secondary infections or thrombosis between the two groups.

Conclusions This systematic review and meta-analysis found that the addition of tocilizumab to the SOC might reduce mortality after 14 days in patients with COVID-19, particularly critical patients requiring MV. More extensive RCTs with longer follow-up periods are needed to validate these findings.

Full Text

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Figures

Figure 1

PRISMA diagram showing selection of articles for review. TCZ: Tocilizum ab, NA: not available.

2A Mortality (≤ 14 days)

2B Mortality (> 14 days)

2C Rate of requirement for mechanical ventilation

Figure 2

The forest plot of synthesis of primary outcomes in TCZ group versus SOC group. Subgroup analysis

Figure 3

The forest plot of mortality stratified by disease severity. MV, mechanical ventilation; TCZ, tocilizumab; SOC, standard of care

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